KANSAS DRUG UTILIZATION REVIEW NEWSLETTER

Health Information Designs, LLC ***1st Quarter 2019***

Welcome to the Quarterly edition of the "Kansas Drug Utilization Review Newsletter," published by Health Information Designs, LLC (HID). This newsletter is part of a continuing effort to keep the Medicaid provider community informed of important changes in the Kansas Medical Assistance Program (KMAP).

Helpful Web Sites

KMAP Web Site
https://www.kmap-state-ks.us/

KDHE-DHCF Web Site
http://www.kdheks.gov/hcf/

KanCare Web Site
http://www.kancare.ks.gov/

Fee-For-Service (FFS) Helpful Numbers

Provider Customer Service (Provider Use Only)
1-800-933-6593

Beneficiary Customer Service
1-800-766-9012

KMAP PA Help Desk
1-800-285-4978

In This Issue:

Overview of Endometriosis and its Treatment

Overview of Endometriosis: Epidemiology, Etiology, and Symptoms

Endometriosis is a medical condition that affects approximately 11 percent of women which results in the growth of endometrial tissue outside of the uterus. Abnormal endometrium growth is commonly found on the ovaries, fallopian tubes, and ligaments that support the uterus; however, it can also occur in the lungs, thighs, arms and other areas beyond the reproductive organs or lower abdomen, which is rare.

The exact cause of endometriosis is unknown but the most widely accepted hypothesis for the pathophysiology of endometriosis is that endometrial cells are transported from the uterine cavity during menstruation and subsequently become implanted at ectopic sites. There are numerous factors that may play a role in the exact etiology and pathophysiology of endometriosis including genetics, hormones, immune cells, and cytokine signaling which are still being researched.

In endometriosis, endometrial tissue develops into growths, called implants, which respond to the menstrual cycle the same that they would inside the uterus. This results in the tissue building up, breaking down, then shedding each month. However, unlike the tissue that lines the inside of the uterus, this tissue cannot be easily discharged from the body, causing inflammation, swelling, the formation of scar tissue or internal bleeding. While it is possible that women with endometriosis may experience no symptoms, most experience a range of painful symptoms due to these endometrial growths. These symptoms can include the following:

- Painful and heavy menstrual cycles
- Chronic pain in the lower back and pelvis
- Pain during or after sexual intercourse
- Intestinal pain
- Painful bowel movements or pain when urinating during menstrual periods
- Blood in the stool or urine
- Bleeding or spotting between menstrual periods
- Excessive bleeding
- Infertility
- Digestive problems (diarrhea, constipation, bloating, or nausea)

Overview of Endometriosis and its Treatment

Overview of Endometriosis: Diagnosis Pharmacological Treatment

The symptoms of endometriosis typically present during reproductive years- on average between the ages of 12 to 60 years old, with most cases diagnosed between the ages of 25 to 35 years of age. Often, there can be a lack of symptoms of endometriosis or less severe symptoms can be mistaken for being normal. This can result in undiagnosed endometriosis until the patient experiences issues with fertility. A suspected diagnosis of endometriosis usually begins after symptoms are experienced. A pelvic examination is done to look for cysts or scar tissue behind the uterus. Additionally, ultrasounds and/or magnetic resonance imaging (MRI) can be useful. While the findings of these imaging and examination techniques may be adequate to suspect a diagnosis of endometriosis and begin empiric therapy, a definitive diagnosis of endometriosis can only be confirmed after laparoscopic surgery.

Pharmacological Treatment of Endometriosis Pain

Currently there is no cure for endometriosis, therefore pharmacological treatment of endometriosis is primarily directed at controlling pain symptoms caused by endometrial implant growth. Medications commonly recommended for controlling endometriosis pain can be broadly categorized into two groups: 1) oral analgesics for adjunctive pain control, such as nonsteroidal anti-inflammatory drugs (NSAIDs); and 2) hormone-based therapies, which includes 5 classes of medications that reduce endometriosis pain through their effects on endometrial tissue, which are listed below. As in all cases, selection of an agent should be done in a patient-centered, evidence-driven manner. Important and major considerations for each class are included below. Please note that this list is not all-inclusive and careful consideration should be made when determining the appropriate therapy to treat endometriosis pain.

- **Combination estrogen and progestin contraceptive agents**
  - **Mechanism**: Exogenous sources of estrogen and progesterone reduce gonadotropin-releasing hormone (GnRH) secretion resulting in reduced pituitary follicle-stimulating hormone (FSH) and luteinizing hormone (LH) secretions, which in turn lead to reduced estrogen production. This causes reduced estrogen activity and growth at endometrial tissues.
  - **Considerations**: Risk of thrombotic events; risk of cardiovascular (CV) disease.
- **Progestin only agents [depot medroxyprogesterone & norethindrone]:**
  - **Mechanism**: Progestins stop endometrial cell proliferation, causing endometrial tissue atrophy and allowing organized sloughing of endometrial cells.
  - **Considerations**: May cause loss in bone mineral density (BMD); risk of thrombotic events; may exacerbate migraine.
- **GnRH agonists [Zoladex (goserelin), Lupron Depot (leuprolide), & Synarel (nafarelin)]:**
  - **Mechanism**: Prolonged use results in GnRH receptor over-stimulation and desensitization, resulting in highly reduced FSH and LH secretions, leading to significantly reduced estrogen production. This deprives endometrial tissues of estrogen, causing them to become inactive and degenerate.
  - **Considerations**: May cause reduced BMD; may cause or worsen CV disease; exacerbation of endometriosis symptoms may occur after the first dose.
- **Androgens (Danazol):**
  - **Mechanism**: Suppresses pituitary output of follicle-stimulating hormone (FSH) and luteinizing hormone (LH), resulting in regression and atrophy of normal and ectopic endometrial tissue.
  - **Considerations**: High incidence of multiple adverse events reported and thus should be reserved for use only when other agents are not available.
- **GnRH antagonists [Orilissa (elagolix)]:**
  - **Mechanism:** Blocks pituitary GnRH receptors, ultimately resulting in the same effects on endometrial tissue via estrogen deprivation.
  - **Considerations**: Reviewed on next page.

Orilissa (elagolix)

Orilissa (elagolix), was FDA-approved on July 24, 2018 as the first oral gonadotropin-releasing hormone (GnRH) antagonist specifically indicated for the treatment of moderate to severe endometriosis pain. The FDA approval was based on data from two double-blind, placebo-controlled studies in 1,686 women with moderate to severe pain associated with endometriosis. The results of the studies indicated that treatment with Orilissa versus those treated with placebo resulted in significant reductions in daily menstrual pelvic pain, non-menstrual pelvic pain and pain with sex, as well as significant reduction in endometriosis pain from baseline scores compared to placebo at month three. Information for consideration regarding Orilissa's recommended dosing, contraindications, and warnings/precautions is summarized below.

Dosing and Administration: Due to its ability to cause a duration and dose-dependent decrease in bone mineral density (BMD), use of Orilissa should be limited to the recommended dosing and duration. These recommendations consist of one of the following:

- 150 mg once daily for up to 24 months
- 200 mg twice daily for up to 6 months
- 150 mg once daily for up to 6 months for women with moderate hepatic impairment

Contraindications: Pregnancy; known osteoporosis; severe hepatic impairment; concomitant use of strong organic anion transporting polypeptide 1B1 inhibitors (e.g. cyclosporine, gemfibrozil, etc).

Warnings and Precautions:

- Orilissa can cause menstrual bleeding irregularities including decreases in the amount, intensity or duration of bleeding which may alter the ability to detect pregnancy. Discontinue use if pregnancy is confirmed.
- A dose-dependent decrease in BMD is associated with Orilissa exposure and may not be completely reversible following discontinuation. Because the risk of BMD loss also increases with duration of use, length of treatment should not exceed recommendations and providers should consider supplementation with calcium and vitamin D during treatment.
- Orilissa may increase the risk of depression and mood changes, especially in patients with a history of suicidality or depression. Promptly evaluate new or worsening psychiatric symptoms and refer the patient to a mental health care professional if appropriate.
- Orilissa may cause a dose-dependent elevation of serum alanine aminotransferase (ALT) at least 3-times the upper limit of the reference range. Use the lowest effective dose and instruct patients to promptly seek medical attention for symptoms or signs that may reflect liver injury. Promptly evaluate patients with elevations in liver tests to determine whether the benefits of continued therapy outweigh the risks.
- Estrogen containing contraceptives are expected to reduce the efficacy of Orilissa and the effect of progestin-only contraceptives on efficacy is unknown. Women should use non-hormonal contraceptives during treatment with and for one week after discontinuing Orilissa.

References

1) Orilissa (elagolix) [prescribing information]. North Chicago, IL: AbbVie Inc; July 2018.
2) Schrager S, Falleroni J, Edgoose J. Evaluation and treatment of endometriosis. Am Fam Physician. 2013 Jan 15;87(2):107-13.
3) Armstrong C. ACOG updates guideline on diagnosis and treatment of endometriosis.
4) Facts & Comparisons eAnswers. Available at http://online.factsandcomparisons.com. Accessed on March 15, 2019.
5) Khan SA. Drug therapy for endometriosis-associated pain. US Pharm. 2015 Jan 1;1:21.

Generic Medications

Recently Approved Generic Drugs:

January 2019	February 2019	March 2019
Latuda (lurasidone)	Zovirax 5% cream (acyclovir)	Mestinon syrup (pyridostigmine)
Picato Gel (ingenol gel)	Fetzima (levomilnacipran)	Letairis (ambrisentan)
Sabril (vigabatrin)	Ferriprox (deferiprone)	
Rapamune (sirolimus oral sln)	Iquix ophthalmic sln (levofloxacin)	

Upcoming Generic Drugs:

Generic Name	Brand Name	Anticipated Launch
solifenacin	Vesicare	April 2019
treprostinil	Remodulin	Early 2019
deferasirox	Exjade	Early 2019
pregabalin	Lyrica	July 2019

PRST STD
U.S. Postage

Health Information Designs, LLC
391 Industry Drive
Auburn, AL 36832
www.hidesigns.com

Mailing Address Line 1
Mailing Address Line 2
Mailing Address Line 3
Mailing Address Line 4
Mailing Address Line 5